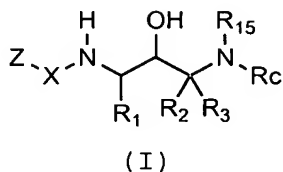


What is claimed is:

1. A compound of formula (I):



5

or a pharmaceutically acceptable salt or ester thereof,  
wherein Z is aryl, heteroaryl or heterocyclyl, wherein said  
groups are optionally substituted with 1 or 2  $R_B$  groups,  
wherein,

- 10 where  $R_B$  at each occurrence is independently selected from  
halogen, -OH, -OCF<sub>3</sub>, -O-phenyl, -CN, -NR<sub>100</sub>R<sub>101</sub>, C<sub>1</sub>-C<sub>6</sub>  
alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, (CH<sub>2</sub>)<sub>0-3</sub>(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), aryl, heteroaryl, or heterocyclyl  
wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl,  
15 aryl, heteroaryl, or heterocyclyl groups are optionally  
substituted with 1 or 2 substituents independently  
selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub>  
alkoxy, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, halogen, -OH, -  
CN, or -NR<sub>100</sub>R<sub>101</sub>;

- 20 where R<sub>100</sub> and R<sub>101</sub> are at each occurrence are  
independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, or phenyl;

X is -(C=O)- or -(SO<sub>2</sub>)-;

- wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1, 2, or  
3 groups independently selected from halogen, -OH, =O, -SH,  
25 -CN, -CF<sub>3</sub>, -OCF<sub>3</sub>, -C<sub>3-7</sub> cycloalkyl, -C<sub>1</sub>-C<sub>4</sub> alkoxy, amino, mono-  
dialkylamino, aryl, heteroaryl, heterocycloalkyl, wherein each  
aryl group is optionally substituted with 1, 2 or 3  $R_{50}$  groups;

- wherein  $R_{50}$  is selected from halogen, OH, SH, CN, -CO-(C<sub>1</sub>-  
C<sub>4</sub> alkyl), -NR<sub>7</sub>R<sub>8</sub>, -S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub>  
30 alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy and C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy and  
cycloalkyl groups are optionally substituted with 1  
or 2 substituents independently selected from the

group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, OH, -NR<sub>5</sub>R<sub>6</sub>,  
CN, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, NR<sub>7</sub>R<sub>8</sub>, and C<sub>1</sub>-C<sub>4</sub> alkoxy;

wherein R<sub>5</sub> and R<sub>6</sub> are independently H or  
C<sub>1</sub>-C<sub>6</sub> alkyl; or

5 wherein R<sub>5</sub> and R<sub>6</sub> and the nitrogen to which  
they are attached form a 5 or 6 membered  
heterocycloalkyl ring; and

wherein R<sub>7</sub> and R<sub>8</sub> are independently  
selected from the group consisting of H; -  
10 C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with 1,  
2, or 3 groups independently selected from  
the group consisting of -OH, -NH<sub>2</sub>, and  
halogen; -C<sub>3</sub>-C<sub>6</sub> cycloalkyl; -(C<sub>1</sub>-C<sub>4</sub> alkyl)-  
O-(C<sub>1</sub>-C<sub>4</sub> alkyl); -C<sub>2</sub>-C<sub>4</sub> alkenyl; and -C<sub>2</sub>-C<sub>4</sub>  
15 alkynyl;

wherein each heteroaryl is optionally substituted with 1  
or 2 R<sub>50</sub> groups;

wherein each heterocycloalkyl group is optionally  
substituted with 1 or 2 groups that are independently R<sub>50</sub>  
20 or =O;

R<sub>2</sub> and R<sub>3</sub> are independently selected from

-H;

-F;

-C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with a substituent  
25 selected from the group consisting of -F, -OH, -C≡N, -  
CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>5</sub>R<sub>6</sub>;

-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>17</sub>;

-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>18</sub>;

-C<sub>2</sub>-C<sub>6</sub> alkenyl or C<sub>2</sub>-C<sub>6</sub> alkynyl, wherein each is optionally  
30 substituted with an independent substituent selected from  
the group consisting of -F, -OH, -C≡N, -CF<sub>3</sub> and C<sub>1</sub>-C<sub>3</sub>  
alkoxy;

-(CH<sub>2</sub>)<sub>0-2</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted an  
independent substituent selected from the group

consisting of -F, -OH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy and -NR<sub>5</sub>R<sub>6</sub>;  
or

R<sub>2</sub>, R<sub>3</sub> and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one  
5 carbon atom is optionally replaced by a group selected from -O-, -S-, -SO<sub>2</sub>-, or -NR<sub>7</sub>-;

where R<sub>17</sub> at each occurrence is an aryl group selected from phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl and tetralinyl,  
10 wherein said aryl groups are optionally substituted with one or two groups that are independently -C<sub>1</sub>-C<sub>3</sub> alkyl; -C<sub>1</sub>-C<sub>4</sub> alkoxy; CF<sub>3</sub>; or -C<sub>2</sub>-C<sub>6</sub> alkenyl or -C<sub>2</sub>-C<sub>6</sub> alkynyl each of which is optionally substituted with one substituent selected  
15 from the group consisting of F, OH, C<sub>1</sub>-C<sub>3</sub> alkoxy; or -halogen;

-OH;  
-C≡N;  
-C<sub>3</sub>-C<sub>7</sub> cycloalkyl;  
20 -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl);  
-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl);

where R<sub>18</sub> is a heteroaryl group selected from pyridinyl, pyrimidinyl, quinolinyl, indolyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl,  
25 quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, oxazolyl, thiazolyl, furanyl, thienyl, pyrrolyl, oxadiazolyl or thiadiazolyl, wherein each of said heteroaryl groups is optionally substituted with one or two groups that are independently

30 -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of OH, C≡N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>5</sub>R<sub>6</sub>;

R<sub>15</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub>  
35 alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub>

alkyl, halo C<sub>1</sub>-C<sub>6</sub> alkyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, NH<sub>2</sub>, and -R<sub>26</sub>-R<sub>27</sub>;

5                    wherein R<sub>26</sub> is selected from the group consisting of a bond, -C(O)-, -SO<sub>2</sub>-, -CO<sub>2</sub>-, -C(O)NR<sub>5</sub>-, and -NR<sub>5</sub>C(O)-

                  , wherein R<sub>27</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, 10 heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, halogen, haloalkyl, hydroxyalkyl, -NR<sub>5</sub>R<sub>6</sub>, -C(O)NR<sub>5</sub>R<sub>6</sub>;

15 R<sub>C</sub> is selected from the group consisting of -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>8</sub>) cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -R<sub>205</sub>, -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), and aryl, wherein aryl is optionally substituted with

20 1 or 2 independently selected R<sub>200</sub> groups;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-aryl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heteroaryl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heterocycloalkyl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-aryl-heteroaryl;

25 - (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-aryl-heterocycloalkyl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-aryl-aryl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heteroaryl-aryl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heteroaryl-heterocycloalkyl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heteroaryl-heteroaryl;

30 - (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heterocycloalkyl-heteroaryl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heterocycloalkyl-heterocycloalkyl;

- (CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub>-heterocycloalkyl-aryl;

- a monocyclic or bicyclic ring of 5, 6, 7 8, 9, or 10 carbons fused to 1 or 2 aryl, heteroaryl, or heterocycloalkyl groups

wherein 1, 2 or 3 carbons of the monocyclic or bicyclic ring is optionally replaced with

-NH,

-N(CO)<sub>0-1</sub>R<sub>215</sub>,

5 -N(CO)<sub>0-1</sub>R<sub>220</sub>,

-O, or

-S(=O)<sub>0-2</sub>,

and wherein the monocyclic or bicyclic ring is optionally substituted with 1, 2 or 3 groups that are independently

10 -R<sub>205</sub>, -R<sub>245</sub>, -R<sub>250</sub> or =O;

-C<sub>2</sub>-C<sub>6</sub> alkenyl optionally substituted with 1, 2, or 3 R<sub>205</sub> groups;

-C<sub>2</sub>-C<sub>6</sub> alkynyl optionally substituted with 1, 2, or 3 R<sub>205</sub> groups;

15 wherein each aryl group attached directly or indirectly to the -(CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub> group is optionally substituted with 1, 2, 3 or 4 R<sub>200</sub> groups;

wherein each heteroaryl group attached directly or indirectly to the -(CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub> group is optionally substituted with 1, 2, 3, or 4 R<sub>200</sub>;

20 wherein each heterocycloalkyl attached directly or indirectly to the -(CR<sub>245</sub>R<sub>250</sub>)<sub>0-4</sub> group is optionally substituted with 1, 2, 3, or 4 R<sub>210</sub>;

wherein R<sub>200</sub> at each occurrence is independently selected from the group consisting of

25 -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with 1, 2, or 3 R<sub>205</sub> groups;

-OH;

-NO<sub>2</sub>;

30 -halogen;

-C≡N;

-(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>220</sub>R<sub>225</sub>;

-(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>8</sub> alkyl);

-(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>8</sub> alkenyl);

35 -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>8</sub> alkynyl);

- (CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);
- (CH<sub>2</sub>)<sub>0-4</sub>-(CO)<sub>0-1</sub>-aryl;
- (CH<sub>2</sub>)<sub>0-4</sub>-(CO)<sub>0-1</sub>-heteroaryl;
- (CH<sub>2</sub>)<sub>0-4</sub>-(CO)<sub>0-1</sub>-heterocycloalkyl;
- 5 - (CH<sub>2</sub>)<sub>0-4</sub>-CO<sub>2</sub>R<sub>215</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>220</sub>R<sub>225</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl);
- (CH<sub>2</sub>)<sub>0-4</sub>-S(O)<sub>0-2</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);
- (CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>215</sub>)-CO<sub>2</sub>R<sub>215</sub>;
- 10 - (CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>215</sub>)-SO<sub>2</sub>-R<sub>220</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>215</sub>)-CO-N(R<sub>215</sub>)<sub>2</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-N(-H or R<sub>215</sub>)-CO-R<sub>220</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>220</sub>R<sub>225</sub>;
- (CH<sub>2</sub>)<sub>0-4</sub>-O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl);
- 15 - (CH<sub>2</sub>)<sub>0-4</sub>-O-(R<sub>215</sub>);
- (CH<sub>2</sub>)<sub>0-4</sub>-S-(R<sub>215</sub>);
- (CH<sub>2</sub>)<sub>0-4</sub>-O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with 1, 2, 3, or 5 -F);
- C<sub>2</sub>-C<sub>6</sub> alkenyl optionally substituted with 1 or 2 R<sub>205</sub>
- 20 groups;
- C<sub>2</sub>-C<sub>6</sub> alkynyl optionally substituted with 1 or 2 R<sub>205</sub>
- groups;
- and
- (CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl;
- 25 wherein each aryl group included within R<sub>200</sub> is optionally substituted with 1, 2, or 3 groups that are independently
- R<sub>205</sub>,
- R<sub>210</sub> or
- C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 1, 2, or 3 groups that
- 30 are independently R<sub>205</sub> or R<sub>210</sub>;
- wherein each heterocycloalkyl group included within R<sub>200</sub> is optionally substituted with 1, 2, or 3 groups that are independently R<sub>210</sub>;

wherein each heteroaryl group included within  $R_{200}$  is optionally substituted with 1, 2, or 3 groups that are independently

- $R_{205}$ ,

5

- $R_{210}$ , or

- $C_1$ - $C_6$  alkyl substituted with 1, 2, or 3 groups that are independently

- $R_{205}$  or

- $R_{210}$ ;

10

wherein  $R_{205}$  at each occurrence is independently selected from the group consisting of

- $C_1$ - $C_6$  alkyl,

- $C_2$ - $C_6$  alkenyl,

15

- $C_2$ - $C_6$  alkynyl,

- $C_1$ - $C_6$  haloalkoxy

-( $CH_2$ )<sub>0-3</sub>( $C_3$ - $C_7$  cycloalkyl)

-halogen,

-( $CH_2$ )<sub>0-6</sub>-OH,

20

-O-phenyl,

-SH,

-( $CH_2$ )<sub>0-6</sub>-C $\equiv$ N,

-( $CH_2$ )<sub>0-6</sub>-C(=O)NR<sub>235</sub>R<sub>240</sub>

-CF<sub>3</sub>,

25

- $C_1$ - $C_6$  alkoxy, and

-NR<sub>235</sub>R<sub>240</sub>,

wherein  $R_{210}$  at each occurrence is independently selected from the group consisting of

30

- $C_1$ - $C_6$  alkyl optionally substituted with 1, 2, or 3  $R_{205}$  groups;

- $C_2$ - $C_6$  alkenyl optionally substituted with 1, 2, or 3  $R_{205}$  groups;

35 - $C_2$ - $C_6$  alkynyl optionally substituted with 1, 2, or 3  $R_{205}$  groups;

5                   -halogen;  
                  -C<sub>1</sub>-C<sub>6</sub> alkoxy;  
                  -C<sub>1</sub>-C<sub>6</sub> haloalkoxy;  
                  -NR<sub>220</sub>R<sub>225</sub>;  
                  -OH;  
                  -C≡N;  
                  -C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted  
with 1, 2, or 3 R<sub>205</sub> groups;  
                  -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl);  
10                  -SO<sub>2</sub>-NR<sub>235</sub>R<sub>240</sub>;  
                  -CO-NR<sub>235</sub>R<sub>240</sub>;  
                  -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl); and  
                  =O; wherein  
                  wherein R<sub>215</sub> at each occurrence is independently selected  
15   from the group consisting of  
                  -C<sub>1</sub>-C<sub>6</sub> alkyl,  
                  -(CH<sub>2</sub>)<sub>0-2</sub>-(aryl),  
                  -C<sub>2</sub>-C<sub>6</sub> alkenyl,  
                  -C<sub>2</sub>-C<sub>6</sub> alkynyl,  
20                  -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
                  -(CH<sub>2</sub>)<sub>0-2</sub>-(heteroaryl), and  
                  -(CH<sub>2</sub>)<sub>0-2</sub>-(heterocycloalkyl);  
                  wherein the aryl group included within R<sub>215</sub> is  
                  optionally substituted with 1, 2, or 3 groups that  
25   are independently  
                  -R<sub>205</sub> or  
                  -R<sub>210</sub>;  
                  wherein the heterocycloalkyl group included within  
                  R<sub>215</sub> is optionally substituted with 1, 2, or 3 R<sub>210</sub>;  
30   wherein each heteroaryl group included within R<sub>215</sub> is  
                  optionally substituted with 1, 2, or 3 R<sub>210</sub>;  
                  wherein R<sub>220</sub> and R<sub>225</sub> at each occurrence are independently  
                  selected from the group consisting of  
                  -H,  
35   -C<sub>1</sub>-C<sub>6</sub> alkyl,



-hydroxy C<sub>1</sub>-C<sub>6</sub> alkyl,  
-amino C<sub>1</sub>-C<sub>6</sub> alkyl,  
-halo C<sub>1</sub>-C<sub>6</sub> alkyl,  
-(CH<sub>2</sub>)<sub>0-2</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),  
5       -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),  
-C<sub>2</sub>-C<sub>6</sub> alkenyl,  
-C<sub>2</sub>-C<sub>6</sub> alkynyl,  
-aryl,  
-heteroaryl, and  
10       -heterocycloalkyl;  
wherein the aryl, heteroaryl or heterocycloalkyl group  
included within R<sub>220</sub> and R<sub>225</sub> is optionally substituted  
with 1, 2, or 3 R<sub>270</sub> groups,  
      wherein R<sub>270</sub> at each occurrence is independently  
15       -R<sub>205</sub>,  
      -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with 1, 2, or 3  
R<sub>205</sub> groups;  
      -C<sub>2</sub>-C<sub>6</sub> alkenyl optionally substituted with 1, 2, or 3  
R<sub>205</sub> groups;  
20       -C<sub>2</sub>-C<sub>6</sub> alkynyl optionally substituted with 1, 2, or 3  
R<sub>205</sub> groups;  
      -halogen;  
      -C<sub>1</sub>-C<sub>6</sub> alkoxy;  
      -C<sub>1</sub>-C<sub>6</sub> haloalkoxy;  
25       -NR<sub>235</sub>R<sub>240</sub>;  
      -OH;  
      -C≡N;  
      -C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted with 1, 2,  
or 3 R<sub>205</sub> groups;  
30       -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl);  
      -SO<sub>2</sub>-NR<sub>235</sub>R<sub>240</sub>;  
      -CO-NR<sub>235</sub>R<sub>240</sub>;  
      -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl); and  
      =O;  
35       wherein R<sub>235</sub> and R<sub>240</sub> at each occurrence are independently

-H, or  
-C<sub>1</sub>-C<sub>6</sub> alkyl;  
-phenyl

wherein R<sub>245</sub> and R<sub>250</sub> at each occurrence are independently  
5 selected from the group consisting of

-H,  
-(CH<sub>2</sub>)<sub>0-4</sub>CO<sub>2</sub>C<sub>1</sub>-C<sub>4</sub> alkyl  
-(CH<sub>2</sub>)<sub>0-4</sub>C(=O)C<sub>1</sub>-C<sub>4</sub> alkyl  
-C<sub>1</sub>-C<sub>4</sub> alkyl,  
10 -C<sub>1</sub>-C<sub>4</sub> hydroxyalkyl,  
-C<sub>1</sub>-C<sub>4</sub> alkoxy,  
-C<sub>1</sub>-C<sub>4</sub> haloalkoxy,  
-(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
-C<sub>2</sub>-C<sub>6</sub> alkenyl,  
15 -C<sub>2</sub>-C<sub>6</sub> alkynyl,  
-(CH<sub>2</sub>)<sub>0-4</sub> aryl,  
-(CH<sub>2</sub>)<sub>0-4</sub> heteroaryl, and  
-(CH<sub>2</sub>)<sub>0-4</sub> heterocycloalkyl, or

wherein R<sub>245</sub> and R<sub>250</sub> are taken together with the carbon to  
20 which they are attached to form a monocycle or bicycle of  
3, 4, 5, 6, 7 or 8 carbon atoms, optionally where 1 or 2  
carbon atoms is replaced by a heteroatom selected from  
the group consisting of

-O-,  
25 -S-,  
-SO<sub>2</sub>-, and  
-NR<sub>220</sub>-;

wherein the aryl, heteroaryl or heterocycloalkyl group  
included within R<sub>245</sub> and R<sub>250</sub> is optionally substituted  
30 with 1, 2, or 3 groups that are independently halogen, C<sub>1-6</sub>  
alkyl, CN or OH;

wherein R<sub>255</sub> and R<sub>260</sub> at each occurrence are independently  
selected from the group consisting of  
-H;

-C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with 1, 2, or 3 R<sub>205</sub> groups;

-(CH<sub>2</sub>)<sub>1-2</sub>-S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl);

5    -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>3</sub>-C<sub>7</sub> cycloalkyl optionally substituted with 1, 2, or 3 R<sub>205</sub> groups;

-(CH<sub>2</sub>)<sub>0-4</sub>-aryl;

-(CH<sub>2</sub>)<sub>0-4</sub> -heteroaryl;

-(CH<sub>2</sub>)<sub>0-4</sub> -heterocycloalkyl;

10       wherein each aryl group included within R<sub>255</sub> and R<sub>260</sub> is optionally substituted with 1, 2, or 3 groups that are independently

-R<sub>205</sub>,

-R<sub>210</sub>, or

15       -C<sub>1</sub>-C<sub>6</sub> alkyl substituted with 1, 2, or 3 groups that are independently

-R<sub>205</sub> or

-R<sub>210</sub>;

20       where each heteroaryl group included within R<sub>255</sub> and R<sub>260</sub> is optionally substituted with 1, 2, 3, or 4 R<sub>200</sub> groups, and

where each heterocycloalkyl group included within R<sub>255</sub> and R<sub>260</sub> is optionally substituted with 1, 2, 3, or 4 R<sub>210</sub> groups.

2. A compound according to claim 1, wherein:

25    Z is aryl or heteroaryl, wherein each ring is independently optionally substituted with 1 or 2 groups independently selected from halogen, -OH, -OCF<sub>3</sub>, -O-phenyl, -CN, -NR<sub>100</sub>R<sub>101</sub>, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, (CH<sub>2</sub>)<sub>0-3</sub>(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), aryl, 30 heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub>

haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, halogen, -OH, -CN, or -  
NR<sub>100</sub>R<sub>101</sub>.

3. A compound according to claim 1, wherein X is -  
5 (C=O)-.

4. A compound according to claim 1, wherein:

R<sub>1</sub> is -C<sub>1</sub>-C<sub>6</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>6</sub> alkyl-heteroaryl, or -C<sub>1</sub>-C<sub>6</sub>  
alkyl-heterocyclyl, wherein each aryl group at each  
10 occurrence is optionally substituted with 1, 2 or 3 R<sub>50</sub>  
groups;

wherein R<sub>50</sub> is independently selected from halogen, OH,  
SH, CN, -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -NR<sub>7</sub>R<sub>8</sub>, -S(O)<sub>0-2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),  
C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, or  
15 C<sub>3</sub>-C<sub>8</sub> cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy, or  
cycloalkyl groups are optionally substituted with 1  
or 2 substituents independently selected from the  
group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, OH, -NR<sub>5</sub>R<sub>6</sub>,  
20 CN, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, NR<sub>7</sub>R<sub>8</sub>, and C<sub>1</sub>-C<sub>4</sub> alkoxy;

wherein R<sub>5</sub> and R<sub>6</sub> at each occurrence are  
independently H or C<sub>1</sub>-C<sub>6</sub> alkyl; or  
wherein R<sub>5</sub> and R<sub>6</sub> and the nitrogen to which  
they are attached, at each occurrence form  
25 a 5 or 6 membered heterocycloalkyl ring;  
and

wherein R<sub>7</sub> and R<sub>8</sub> are independently  
selected from the group consisting of H; -  
C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with 1,  
30 2, or 3 groups independently selected from  
the group consisting of -OH, -NH<sub>2</sub>, and  
halogen; -C<sub>3</sub>-C<sub>6</sub> cycloalkyl; -(C<sub>1</sub>-C<sub>4</sub> alkyl)-  
O-(C<sub>1</sub>-C<sub>4</sub> alkyl); -C<sub>2</sub>-C<sub>4</sub> alkenyl; and -C<sub>2</sub>-C<sub>4</sub>  
alkynyl;

wherein each heteroaryl at each occurrence is optionally substituted with 1 or 2  $R_{50}$  groups;

wherein each heterocycloalkyl group at each occurrence is optionally substituted with 1 or 2 groups that are independently  $R_{50}$  or =O..

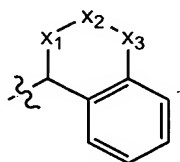
5. A compound according to claim 1, wherein  $R_2$  and  $R_3$  are hydrogen.

6. A compound according to claim 1, wherein  $R_{15}$  is hydrogen.

7. A compound according to claim 1, wherein:

$R_C$  is selected from the group consisting of :  $-(CH_2)_{0-3}-(C_3-C_8)$  cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of  $-R_{205}$ , and  $-CO_2-(C_1-C_4$  alkyl); and a monocyclic or bicyclic ring of 5, 6, 7 8, 9, or 10 carbons fused to 1 or 2 aryl, heteroaryl, or heterocycloalkyl groups wherein 1, 2 or 3 carbons of the monocyclic or bicyclic ring is optionally replaced with  $-NH$ ,  $-N(CO)_{0-1}R_{215}$ ,  $-N(CO)_{0-1}R_{220}$ ,  $-O$ , or  $-S(=O)_{0-2}$ , and wherein the monocyclic or bicyclic ring can be optionally substituted with 1, 2 or 3 groups that are independently  $-R_{205}$   $-R_{245}$ ,  $R_{250}$  or =O.

8. A compound according to claim 1 wherein  $R_C$  is



wherein  $x_1$ ,  $x_2$ , and  $x_3$  are independently  $-CHR_{245}$ ,  $SO_2$ , or  $NH$ , and wherein the phenyl ring is optionally substituted with 1 or 2  $-R_{245}$  groups.

9. A compound according to claim 8 wherein one of  $x_1$ ,  $x_2$ , or  $x_3$  is  $SO_2$ .

5 10. A compound according to claim 8 wherein one of  $x_1$ ,  $x_2$ , or  $x_3$  is NH.

11. A compound according to claim 8 wherein  $x_1$ ,  $x_2$ , and  $x_3$  are each  $CH_2$ .

10

12. A compound according to claim 1 selected from the group consisting of:

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyridine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyrazine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide;

3-amino-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-1,2,4-triazole-5-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-5-methylisoxazole-3-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-6-hydroxypyridine-2-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-imidazole-4-carboxamide;

*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-

hydroxypropyl)nicotinamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1S)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1H-pyrazole-4-carboxamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1S)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)isonicotinamide;

5-chloro-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1S)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)thiophene-2-carboxamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4S)-6-neopentyl-3,4-dihydro-2H-chromen-4-yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(4S)-6-tert-butoxy-3,4-dihydro-2H-chromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4S)-6-neopentyl-1,2,3,4-tetrahydroquinolin-4-yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(4S)-6-tert-butoxy-1,2,3,4-tetrahydroquinolin-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-7-neopentyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(1S)-7-tert-butoxy-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

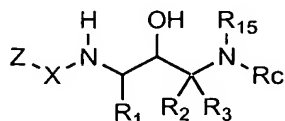
N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4R)-6-neopentyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(4R)-6-tert-butoxy-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-

neopentylphenyl)cyclohexyl]amino}propyl)benzamide;  
 N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclohexyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;  
 N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-neopentylphenyl)cyclopropyl]amino}propyl)benzamide;  
 N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;  
 N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-neopentyl-1,1'-biphenyl-2-yl)methyl]amino}propyl)benzamide;  
 N-[(1S,2R)-3-{[(4-tert-butoxy-1,1'-biphenyl-2-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;  
 N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-neopentyl-9H-fluoren-9-yl)amino]propyl)benzamide;  
 N-[(1S,2R)-3-[(2-tert-butoxy-9H-fluoren-9-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;  
 N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-3,5-dimethylbenzamide; and  
 N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide.

13. A method for making a compound of formula (I)



(I)

or a pharmaceutically acceptable salt or ester thereof, wherein Z, X, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>15</sub> and R<sub>c</sub> are as defined in claim 1.



14. A method for the treatment or prevention of Alzheimer's disease, mild cognitive impairment Down's syndrome, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, cerebral amyloid angiopathy, other  
5 degenerative dementias, dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease comprising  
10 administration of a therapeutically effective amount of a compound or salt according to Claim 1, to a patient in need thereof.

15. A method of treatment as in claim 14, wherein the  
15 patient is a human.

16. A method of treatment according to claim 14, wherein the disease is dementia.

20 17. A pharmaceutical composition comprising a compound according to claim 1 in combination with a physiologically acceptable carrier or excipient.